

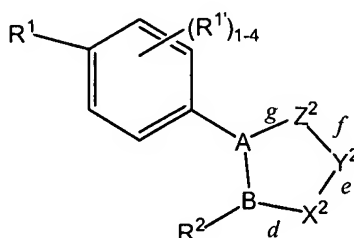
Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1 - 58 (Cancelled)

59. (Previously Presented) A compound of Formula (II), or a pharmaceutically acceptable salt thereof;



II

wherein:

A-B is:

- (a) N-C;
- (b) C-N; or
- (c) N-N;

when sides *e* and *g* are double bonds, and sides *d* and *f* are single bonds,

-X²-Y²-Z²- is:

- (a) -N=CR⁴-CR⁵=; or
- (b) -CR⁴=CR⁵-CR⁵=;

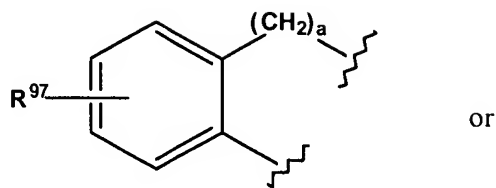
when sides *d* and *f* are double bonds, and sides *e* and *g* are single bonds,

-X²-Y²-Z²- is:

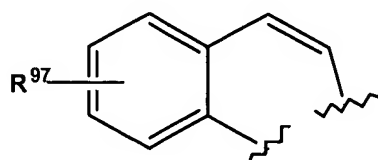
- (a) =CR⁴-CR⁴=CR⁵-;
- (b) =CR⁴-CR⁵=N-; or
- (c) =CR²'-CR⁵=N-;

R² and R²' taken together are:

(a)



(b)



or $R^{2'}$ and R^5 taken together with the carbon atoms to which they are attached are a cycloalkyl group or a heterocyclic ring;

R^{97} is:

- (a) hydrogen;
- (b) alkylthio;
- (c) alkylsulfinyl;
- (d) alkylsulfonyl;
- (e) cyano;
- (f) carboxyl;
- (g) amino;
- (h) lower alkyl;
- (i) haloalkyl;
- (j) hydroxy;
- (k) alkoxy;
- (l) haloalkoxy;
- (m) alkylarylalkylamino;
- (n) aminoalkyl;

Amendment under 37 C.F.R. § 1.312
Application No. 10/608,333

- (o) aminoaryl;
- (p) sulfonamido;
- (q) alkylsulfonamido;
- (r) arylsulfonamido;
- (s) heterocyclic ring;
- (t) hydroxyalkyl; or
- (u) nitro;

a is an integer from 1 to 3;

R¹ is:

- (a) -S(O)₂-CH₃;
- (b) -S(O)₂-NR⁸(D¹); or
- (c) -S(O)(NH)CH₃;

R¹ at each occurrence is independently:

- (a) hydrogen;
- (b) halogen;
- (c) methyl; or
- (d) CH₂OH;

R² is:

- (a) lower alkyl;
- (b) cycloalkyl;
- (c) mono-, di- or tri-substituted phenyl or naphthyl, wherein the substituents are

each independently:

- (1) hydrogen;
- (2) halo;
- (3) alkoxy;
- (4) alkylthio;
- (5) CN;
- (6) haloalkyl, preferably CF₃;
- (7) lower alkyl;

- (8) N_3 ;
- (9) $-CO_2D^1$;
- (10) $-CO_2$ -lower alkyl;
- (11) $-(C(R^5)(R^6))_z-OD^1$;
- (12) $-(C(R^5)(R^6))_z-O$ -lower alkyl;
- (13) lower alkyl- CO_2-R^5 ;
- (14) $-OD^1$;
- (15) haloalkoxy;
- (16) amino;
- (17) nitro;
- (18) alkylsulfinyl; or
- (19) heteroaryl;

(d) mono-, di- or tri-substituted heteroaryl, wherein the heteroaryl is a monocyclic aromatic ring of 5 atoms, said ring having one heteroatom which is S, O, or N, and, optionally, 1, 2, or 3 additional N atoms; or the heteroaryl is a monocyclic ring of 6 atoms, said ring having one heteroatom which is N, and, optionally, 1, 2, 3, or 4 additional N atoms; wherein the substituents are each independently:

- (1) hydrogen;
- (2) halo;
- (3) lower alkyl;
- (4) alkoxy;
- (5) alkylthio;
- (6) CN;
- (7) haloalkyl, preferably CF_3 ;
- (8) N_3 ;
- (9) $-C(R^5)(R^6)-OD^1$;
- (10) $-C(R^5)(R^6)-O$ -lower alkyl; or
- (11) alkylsulfinyl;

(e) benzoheteroaryl which includes the benzo fused analogs of (d);

(f) $-NR^{10}R^{11}$;

(g) $-SR^{11}$;

(h) $-OR^{11}$;

(i) $-R^{11}$;

(j) alkenyl;

(k) alkynyl;

(l) unsubstituted, mono-, di-, tri- or tetra-substituted cycloalkenyl, wherein the substituents are each independently:

(1) halo;

(2) alkoxy;

(3) alkylthio;

(4) CN;

(5) haloalkyl, preferably CF_3 ;

(6) lower alkyl;

(7) N_3 ;

(8) $-CO_2D^1$;

(9) $-CO_2$ -lower alkyl;

(10) $-C(R^{12})(R^{13})-OD^1$;

(11) $-C(R^{12})(R^{13})-O$ -lower alkyl;

(12) lower alkyl- CO_2-R^{12} ;

(13) benzyloxy;

(14) $-O$ -(lower alkyl)- CO_2R^{12} ;

(15) $-O$ -(lower alkyl)- $NR^{12}R^{13}$; or

(16) alkylsulfinyl;

(m) mono-, di-, tri- or tetra-substituted heterocycloalkyl group of 5, 6 or 7 members, or a benzoheterocycle, wherein said heterocycloalkyl or benzoheterocycle contains 1 or 2 heteroatoms selected from O, S, or N and, optionally, contains a carbonyl group or a sulfonyl group, and wherein said substituents are each independently:

(1) halo;

- (2) lower alkyl;
- (3) alkoxy;
- (4) alkylthio;
- (5) CN;
- (6) haloalkyl, preferably CF₃;
- (7) N₃;
- (8) -C(R¹²)(R¹³)-OD¹;
- (9) -C(R¹²)(R¹³)-O-lower alkyl; or
- (10) alkylsulfinyl;

(n) styryl, mono or di-substituted styryl, wherein the substituent are each independently:

- (1) halo;
- (2) alkoxy;
- (3) alkylthio;
- (4) CN;
- (5) haloalkyl, preferably CF₃;
- (6) lower alkyl;
- (7) N₃;
- (8) -CO₂D¹;
- (9) -CO₂-lower alkyl;
- (10) -C(R¹²)(R¹³)-OD¹;
- (11) -C(R¹²)(R¹³)-O-lower alkyl;
- (12) lower alkyl-CO₂-R¹² ;
- (13) benzyloxy;
- (14) -O-(lower alkyl)-CO₂R¹²; or
- (15) -O-(lower alkyl)-NR¹²R¹³ ;

(o) phenylacetylene, mono- or di-substituted phenylacetylene, wherein the substituents are each independently:

- (1) halo;

- (2) alkoxy;
- (3) alkylthio;
- (4) CN;
- (5) haloalkyl, preferably CF₃;
- (6) lower alkyl;
- (7) N₃;
- (8) -CO₂D¹;
- (9) -CO₂-lower alkyl;
- (10) -C(R¹²)(R¹³)-OD¹;
- (11) -C(R¹²)(R¹³)-O-lower alkyl;
- (12) lower alkyl-CO₂-R¹²;
- (13) benzyloxy;
- (14) -O-(lower alkyl)-CO₂R¹²; or
- (15) -O-(lower alkyl)-NR¹²R¹³;

(p) fluoroalkenyl;

(q) mono- or di-substituted bicyclic heteroaryl of 8, 9 or 10 members, containing 2, 3, 4 or 5 heteroatoms, wherein at least one heteroatom resides on each ring of said bicyclic heteroaryl, said heteroatoms are each independently O, S and N and said substituents are each independently:

- (1) hydrogen;
- (2) halo;
- (3) lower alkyl;
- (4) alkoxy;
- (5) alkylthio;
- (6) CN;
- (7) haloalkyl, preferably CF₃;
- (8) N₃;
- (9) -C(R⁵)(R⁶)-OD¹; or
- (10) -C(R⁵)(R⁶)-O-lower alkyl;

Amendment under 37 C.F.R. § 1.312
Application No. 10/608,333

- (r) K;
- (s) aryl;
- (t) arylalkyl;
- (u) cycloalkylalkyl;
- (v) $-C(O)R^{11}$;
- (u) hydrogen;
- (v) arylalkenyl;
- (w) arylalkoxy;
- (x) alkoxy;
- (y) aryloxy;
- (z) cycloalkoxy;
- (aa) arylthio;
- (bb) alkylthio;
- (cc) arylalkylthio; or
- (dd) cycloalkylthio;

R^4 , $R^{4'}$, R^5 and $R^{5'}$ are each independently:

- (a) hydrogen;
- (b) amino;
- (c) CN;
- (d) lower alkyl;
- (e) haloalkyl;
- (f) alkoxy;
- (g) alkylthio;
- (h) Q;
- (i) $-O-Q$;
- (j) $-S-Q$;
- (k) K;
- (l) cycloalkoxy;
- (m) cycloalkylthio;

(n) unsubstituted, mono-, or di-substituted phenyl or unsubstituted, mono-, or di-substituted benzyl, wherein the substituents are each independently:

- (1) halo;
- (2) lower alkyl;
- (3) alkoxy;
- (4) alkylthio;
- (5) CN;
- (6) haloalkyl, preferably CF₃;
- (7) N₃;
- (8) Q;
- (9) nitro; or
- (10) amino;

(o) unsubstituted, mono-, or di-substituted heteroaryl or unsubstituted, mono-, or di-substituted heteroarylmethyl, wherein the heteroaryl is a monocyclic aromatic ring of 5 atoms, said ring having one heteroatom which is S, O, or N, and, optionally, 1, 2, or 3 additional N atoms; or the heteroaryl is a monocyclic ring of 6 atoms, said ring having one heteroatom which is N, and, optionally, 1, 2, 3, or 4 additional N atoms; said substituents are each independently:

- (1) halo;
- (2) lower alkyl;
- (3) alkoxy;
- (4) alkylthio;
- (5) CN;
- (6) haloalkyl, preferably CF₃;
- (7) N₃;
- (8) -C(R⁶)(R⁷)-OD¹;
- (9) -C(R⁶)(R⁷)-O-lower alkyl; or
- (10) alkylsulfinyl

(p) -CON(R⁸)(R⁸);

(q) -CH₂OR⁸;

(r) $-\text{CH}_2\text{OCN}$;

(s) unsubstituted or substituted:

- (1) lower alkyl-Q;
- (2) -O-lower alkyl-Q;
- (3) -S-lower alkyl-Q;
- (4) lower alkyl-O-lower alkyl-Q;
- (5) lower alkyl-S-lower alkyl-Q;
- (6) lower alkyl-O-Q;
- (7) lower alkyl-S-Q;
- (8) lower alkyl-O-K;
- (9) lower alkyl-S-K;
- (10) lower alkyl-O-V; or
- (11) lower alkyl-S-V;

wherein the substituent(s) resides on the lower alkyl;

(t) cycloalkyl;

(u) aryl;

(v) arylalkyl;

(w) cycloalkylalkyl;

(x) aryloxy;

(y) arylalkoxy;

(z) arylalkylthio;

(aa) cycloalkylalkoxy;

(bb) heterocycloalkyl;

(cc) alkylsulfonyloxy;

(dd) alkylsulfonyl;

(ee) arylsulfonyl;

(ff) arylsulfonyloxy;

(gg) $-\text{C}(\text{O})\text{R}^{10}$;

(hh) nitro;

- (ii) amino;
- (jj) aminoalkyl;
- (kk) -C(O)-alkyl-heterocyclic ring;
- (ll) halo;
- (mm) heterocyclic ring;
- (nn) -CO₂D¹;
- (oo) carboxyl;
- (pp) amidyl; or
- (qq) alkoxyalkyl;

alternatively, R⁴ and R⁵ together with the carbons to which they are attached are:

- (a) cycloalkyl;
- (b) aryl; or
- (c) heterocyclic ring;

alternatively, R⁴ and R^{4'} or R⁵ and R^{5'} taken together with the carbon to which they are attached are:

- (a) cycloalkyl; or
- (b) heterocyclic ring;

alternatively, R⁴ and R⁵, R^{4'} and R^{5'}, R⁴ and R^{5'}, or R^{4'} and R⁵ when substituents on adjacent carbon atoms taken together with the carbons to which they are attached are:

- (a) cycloalkyl;
- (b) heterocyclic ring; or
- (c) aryl;

R⁶ and R⁷ are each independently:

- (a) hydrogen;
- (b) unsubstituted, mono- or di-substituted phenyl; unsubstituted, mono- or di-substituted benzyl; unsubstituted, mono- or di-substituted heteroaryl; mono- or di-substituted heteroarylmethyl, wherein said substituents are each independently:

- (1) halo;
- (2) lower alkyl;

- (3) alkoxy;
- (4) alkylthio;
- (5) CN;
- (6) haloalkyl, preferably CF₃;
- (7) N₃;
- (8) -C(R¹⁴)(R¹⁵)-OD¹; or
- (9) -C(R¹⁴)(R¹⁵)-O-lower alkyl;

- (c) lower alkyl;
- (d) -CH₂OR⁸;
- (e) CN;
- (f) -CH₂CN;
- (g) haloalkyl, preferably fluoroalkyl;
- (h) -CON(R⁸)(R⁸);
- (i) halo; or
- (j) -OR⁸;

R⁸ is:

- (a) hydrogen;
- (b) K; or
- (c) R⁹;

alternatively, R⁵ and R⁵_i, R⁶ and R⁷ or R⁷ and R⁸ together with the carbon to which they are attached form a saturated monocyclic ring of 3, 4, 5, 6 or 7 atoms; optionally containing up to two heteroatoms selected from oxygen, S(O)₀ or NR_i;

R⁹ is:

- (a) lower alkyl;
- (b) lower alkyl-CO₂D¹;
- (c) lower alkyl-NHD¹;
- (d) phenyl or mono-, di- or tri-substituted phenyl, wherein the substituents are

each independently:

- (1) halo;

- (2) lower alkyl;
- (3) alkoxy;
- (4) alkylthio;
- (5) lower alkyl-CO₂D¹;
- (6) lower alkyl-NHD¹;
- (7) CN;
- (8) CO₂D¹; or
- (9) haloalkyl, preferably fluoroalkyl;

(e) benzyl, mono-, di- or tri-substituted benzyl, wherein the substituents are each independently:

- (1) halo;
- (2) lower alkyl;
- (3) alkoxy;
- (4) alkylthio;
- (5) lower alkyl-CO₂D¹;
- (6) lower alkyl-NHD¹;
- (7) CN;
- (8) -CO₂D¹; or
- (9) haloalkyl, preferably CF₃;

(f) cycloalkyl;

(g) K; or

(h) benzoyl, mono-, di-, or trisubstituted benzoyl, wherein the substituents are each independently:

- (1) halo;
- (2) lower alkyl;
- (3) alkoxy;
- (4) alkylthio;
- (5) lower alkyl-CO₂D¹;
- (6) lower alkyl-NHD¹;

(7) CN;

(8) $-\text{CO}_2\text{D}^1$; or

(9) haloalkyl, preferably CF_3 ;

R^{10} and R^{10} , are each independently:

(a) hydrogen; or

(b) R^{11} ;

R^{11} is:

(a) lower alkyl;

(b) cycloalkyl;

(c) unsubstituted, mono-, di- or tri-substituted phenyl or naphthyl, wherein the substituents are each independently:

(1) halo;

(2) alkoxy;

(3) alkylthio;

(4) CN;

(5) haloalkyl, preferably CF_3 ;

(6) lower alkyl;

(7) N_3 ;

(8) $-\text{CO}_2\text{D}^1$;

(9) $-\text{CO}_2$ -lower alkyl;

(10) $-\text{C}(\text{R}^{12})(\text{R}^{13})-\text{OD}^1$;

(11) $-\text{C}(\text{R}^{12})(\text{R}^{13})-\text{O}$ -lower alkyl;

(12) lower alkyl- CO_2D^1 ;

(13) lower alkyl- CO_2R^{12} ;

(14) benzyloxy;

(15) $-\text{O}$ -(lower alkyl)- CO_2D^1 ;

(16) $-\text{O}$ -(lower alkyl)- CO_2R^{12} ; or

(17) $-\text{O}$ -(lower alkyl)- $\text{NR}^{12}\text{R}^{13}$;

(d) unsubstituted, mono-, di- or tri-substituted heteroaryl, wherein the heteroaryl is a monocyclic aromatic ring of 5 atoms, said ring having one heteroatom which is S, O, or N, and, optionally, 1, 2, or 3 additional N atoms; or said heteroaryl is a monocyclic ring of 6 atoms, said ring having one heteroatom which is N, and, optionally 1, 2, or 3 additional N atoms, and wherein said substituents are each independently:

- (1) halo;
- (2) lower alkyl;
- (3) alkoxy;
- (4) alkylthio;
- (5) CN;
- (6) haloalkyl, preferably CF₃;
- (7) N₃;
- (8) -C(R¹²)(R¹³)-OD¹; or
- (9) -C(R¹²)(R¹³)-O-lower alkyl;

(e) unsubstituted, mono- or di-substituted benzoheterocycle, wherein the benzoheterocycle is a 5, 6, or 7-membered ring which contains 1 or 2 heteroatoms independently selected from O, S, or N, and, optionally, a carbonyl group or a sulfonyl group, wherein said substituents are each independently:

- (1) halo;
- (2) lower alkyl;
- (3) alkoxy;
- (4) alkylthio;
- (5) CN;
- (6) haloalkyl, preferably CF₃;
- (7) N₃;
- (8) -C(R¹²)(R¹³)-OD¹; or
- (9) -C(R¹²)(R¹³)-O-lower alkyl;

(f) unsubstituted, mono- or di-substituted benzocarbocycle, wherein the carbocycle is a 5, 6, or 7-membered ring which optionally contains a carbonyl group, wherein said substituents are each independently :

- (1) halo;
- (2) lower alkyl;
- (3) alkoxy;
- (4) alkylthio;
- (5) CN;
- (6) haloalkyl, preferably CF₃;
- (7) N₃;
- (8) -C(R¹²)(R¹³)-OD¹; or
- (9) -C(R¹²)(R¹³)-O-lower alkyl;

(g) hydrogen; or

(h) K

R¹² and R¹³ are each independently:

- (a) hydrogen;
- (b) lower alkyl; or
- (c) aryl; or

R¹² and R¹³ together with the atom to which they are attached form a saturated monocyclic ring of 3, 4, 5, 6 or 7 atoms;

R¹⁴ and R¹⁵ are each independently :

- (a) hydrogen; or
- (b) lower alkyl; or

R¹⁴ and R¹⁵ together with the atom to which they are attached form a carbonyl, a thial, or a saturated monocyclic ring of 3, 4, 5, 6 or 7 atoms;

D¹ is:

- (a) hydrogen or
- (b) D;

D is:

Amendment under 37 C.F.R. § 1.312

Application No. 10/608,333

(a) V; or

(b) K;

U is:

(a) oxygen;

(b) sulfur; or

(c) $-N(R_a)(R_i)-$;

V is:

(a) $-NO$;

(b) $-NO_2$; or

(c) hydrogen

K is $-W_{aa}-E_b-(C(R_e)(R_f))_p-E_c-(C(R_e)(R_f))_x-W_d-(C(R_e)(R_f))_y-W_i-E_j-W_g-(C(R_e)(R_f))_z-U-V$;

wherein aa, b, c, d, g, i and j are each independently an integer from 0 to 3;

p, x, y and z are each independently an integer from 0 to 10;

W at each occurrence is independently:

(a) $-C(O)-$;

(b) $-C(S)-$;

(c) $-T-$;

(d) $-(C(R_e)(R_f))_h-$;

(e) alkyl;

(f) aryl;

(g) heterocyclic ring;

(h) arylheterocyclic ring, or

(i) $-(CH_2CH_2O)_q-$;

E at each occurrence is independently:

(a) $-T-$;

(b) alkyl;

(c) aryl;

(d) $-(C(R_e)(R_f))_h-$;

(e) heterocyclic ring;

Amendment under 37 C.F.R. § 1.312
Application No. 10/608,333

(f) arylheterocyclic ring; or

(g) $-(\text{CH}_2\text{CH}_2\text{O})_q-$;

h is an integer from 1 to 10;

q is an integer from 1 to 5;

R_e and R_f are each independently:

(a) hydrogen;

(b) alkyl;

(c) cycloalkoxy;

(d) halogen;

(e) hydroxy;

(f) hydroxyalkyl;

(g) alkoxyalkyl;

(h) arylheterocyclic ring;

(i) cycloalkylalkyl;

(j) heterocyclicalkyl;

(k) alkoxy;

(l) haloalkoxy;

(m) amino;

(n) alkylamino;

(o) dialkylamino;

(p) arylamino;

(q) diarylamino;

(r) alkylarylamino;

(s) alkoxyhaloalkyl;

(t) haloalkoxy;

(u) sulfonic acid;

(v) alkylsulfonic acid;

(w) arylsulfonic acid;

(x) arylalkoxy;

Amendment under 37 C.F.R. § 1.312
Application No. 10/608,333

- (y) alkylthio;
- (z) arylthio;
- (aa) cyano;
- (bb) aminoalkyl;
- (cc) aminoaryl;
- (dd) alkoxy;
- (ee) aryl;
- (ff) arylalkyl;
- (gg) carboxamido;
- (hh) alkylcarboxamido;
- (ii) arylcarboxamido;
- (jj) amidyl;
- (kk) carboxyl;
- (ll) carbamoyl;
- (mm) alkylcarboxylic acid;
- (nn) arylcarboxylic acid;
- (oo) alkylcarbonyl;
- (pp) arylcarbonyl;
- (qq) ester;
- (rr) carboxylic ester;
- (ss) alkylcarboxylic ester;
- (tt) arylcarboxylic ester;
- (uu) haloalkoxy;
- (vv) sulfonamido;
- (ww) alkylsulfonamido;
- (xx) arylsulfonamido;
- (yy) alkylsulfonyl,
- (zz) alkylsulfonyloxy,
- (aaa) arylsulfonyl,

Amendment under 37 C.F.R. § 1.312
Application No. 10/608,333

- (bbb) arylsulphonyloxy
- (ccc) sulfonic ester;
- (ddd) carbamoyl;
- (eee) urea;
- (fff) nitro;
- (ggg) -U-V; or
- (hhh) $-(C(R'_e)(R'_f))_k-U-V$ or

R'_e and R'_f taken together are:

- (a) oxo;
- (b) thial;
- (c) oxime; or
- (d) hydrazone;

R'_e and R'_f taken together with the carbon atom to which they are attached are:

- (a) heterocyclic ring;
- (b) cycloalkyl group; or
- (c) bridged cycloalkyl group;

R'_e and R'_f are each independently selected from R_e ;

k is an integer from 1 to 3;

T at each occurrence is independently:

- (a) a covalent bond,
- (b) carbonyl,
- (c) an oxygen,
- (d) $-S(O)_o-$; or
- (e) $-N(R_a)(R_i)-$;

o is an integer from 0 to 2;

Q is:

- (a) $-C(O)-U-D^1$;
- (b) $-CO_2$ -lower alkyl;
- (c) tetrazolyl-5-yl;

Amendment under 37 C.F.R. § 1.312
Application No. 10/608,333

- (d) $-C(R^7)(R^8)(S-D^1)$;
- (e) $-C(R^7)(R^8)(O-D^1)$; or
- (f) $-C(R^7)(R^8)(O\text{-lower alkyl})$;

R_a is:

- (a) a lone pair of electron;
- (b) hydrogen; or
- (c) lower alkyl;

R_i is:

- (a) hydrogen;
- (b) alkyl;
- (c) aryl;
- (d) alkylcarboxylic acid;
- (e) arylcarboxylic acid;
- (f) alkylcarboxylic ester;
- (g) arylcarboxylic ester;
- (h) alkylcarboxamido;
- (i) arylcarboxamido;
- (j) alkylsulfinyl;
- (k) alkylsulfonyl;
- (l) alkylsulfonyloxy,
- (m) arylsulfinyl;
- (n) arylsulfonyl;
- (o) arylsulphonyloxy;
- (p) sulfonamido;
- (q) carboxamido;
- (r) carboxylic ester;
- (s) aminoalkyl;
- (t) aminoaryl;
- (u) $-\text{CH}_2-\text{C}(\text{U}-\text{V})(R_e)(R_f)$;

(v) a bond to an adjacent atom creating a double bond to that atom; or

(w) $-(N_2O_2)^- \cdot M^+$, wherein M^+ is an organic or inorganic cation;

with the proviso that the compound of Formula (II) must contain one hydrazone group at position Y_2 .

60. (Previously Presented) A composition comprising the compound of claim 59 and a pharmaceutically acceptable carrier.

61. (Previously Presented) A method for treating or reducing inflammation, pain or fever as a result of elevated levels of COX-2 in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 60.

62 - 63 (Cancelled)

64. (Previously Presented) A method for facilitating wound healing in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 60.

65. (Previously Presented) The method of claim 64, wherein the wound is an ulcer.

66. (Previously Presented) A method for treating or reversing renal and/or respiratory toxicity in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 60.

67 - 70 (Cancelled)

71. (Previously Presented) A method for inhibiting platelet aggregation in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 60.

72. (Previously Presented) The composition of claim 60, further comprising at least one therapeutic agent.

73. (Previously Presented) The composition of claim 72, wherein the therapeutic agent is a steroid, a nonsteroidal antiinflammatory compound, a 5-lipoxygenase (5-LO) inhibitor, a leukotriene B_4 receptor antagonist, a leukotriene A_4 hydrolase inhibitor, a 5-HT agonist, a 3-hydroxy-3-methylglutaryl coenzyme A inhibitor, a H_2 antagonist, an antineoplastic agent, an antiplatelet agent, a thrombin inhibitor, a thromboxane inhibitor, a decongestant, a diuretic, a sedating or non-sedating anti-histamine, an inducible nitric oxide synthase inhibitor,

Amendment under 37 C.F.R. § 1.312
Application No. 10/608,333

an opioid, an analgesic, a *Helicobacter pylori* inhibitor, a proton pump inhibitor, an isoprostane inhibitor, or a mixture of two or more thereof.

74. (Previously Presented) The composition of claim 73, wherein the nonsteroidal antiinflammatory compound is acetaminophen, aspirin, diclofenac, ibuprofen, ketoprofen or naproxen.

75. (Previously Presented) A method for treating or reducing inflammation, pain or fever as a result of elevated levels of COX-2 in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 72.

76 - 77 (Cancelled)

78. (Previously Presented) A method for facilitating wound healing in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 72.

79. (Previously Presented) The method of claim 78, wherein the wound is an ulcer.

80. (Previously Presented) A method for treating or reversing renal and/or respiratory toxicity in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 72.

81-84 (Cancelled)

85. (Previously Presented) A method for inhibiting platelet aggregation in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 72.

86-88 (Cancelled)

89. (Currently Amended) The composition comprising a compound of claim 59 and at least one compound selected from ~~S-nitrosothiol~~ is S-nitroso-N-acetylcysteine, S-nitroso-captopril, S-nitroso-N-acetylpenicillamine, S-nitroso-homocysteine, S-nitroso-cysteine, S-nitroso-glutathione, or S-nitroso-cysteinyl-glycine.

90. (Currently Amended) The composition comprising a compound of claim 59 and at least one compound selected from~~The composition of claim 88, wherein the S-nitrosothiol is:~~

(i) $\text{HS}(\text{C}(\text{R}_e)(\text{R}_f))_m\text{SNO}$;

(ii) $\text{ONS}(\text{C}(\text{R}_e)(\text{R}_f))_m\text{R}_e$; or

(iii) $\text{H}_2\text{N}-\text{CH}(\text{CO}_2\text{H})-(\text{CH}_2)_m-\text{C}(\text{O})\text{NH}-\text{CH}(\text{CH}_2\text{SNO})-\text{C}(\text{O})\text{NH}-\text{CH}_2-\text{CO}_2\text{H}$;

wherein m is an integer from 2 to 20; R_e and R_f are each independently a hydrogen, an alkyl, a cycloalkoxy, a halogen, a hydroxy, an hydroxyalkyl, an alkoxyalkyl, an arylheterocyclic ring, a cycloalkylalkyl, a heterocyclicalkyl, an alkoxy, a haloalkoxy, an amino, an alkylamino, a dialkylamino, an arylamino, a diarylamino, an alkylarylamino, an alkoxyhaloalkyl, a haloalkoxy, a sulfonic acid, a sulfonic ester, an alkylsulfonic acid, an arylsulfonic acid, an arylalkoxy, an alkylthio, an arylthio, a cyano, an aminoalkyl, an aminoaryl, an aryl, an arylalkyl, a carboxamido, a alkylcarboxamido, an arylcarboxamido, an amidyl, a carboxyl, a carbamoyl, an alkylcarboxylic acid, an arylcarboxylic acid, an alkylcarbonyl, an arylcarbonyl, an ester, a carboxylic ester, an alkylcarboxylic ester, an arylcarboxylic ester, a haloalkoxy, a sulfonamido, an alkylsulfonamido, an arylsulfonamido, an alkylsulfonyl, an alkylsulfonyloxy, an arylsulfonyl, an arylsulfonyloxy, a urea, a nitro, $-\text{T}-\text{Q}'$ -, or $-(\text{C}(\text{R}_g)(\text{R}_h))_k-\text{T}-\text{Q}'$ or R_e and R_f taken together are an oxo, a methanthial, a heterocyclic ring, a cycloalkyl group, an oxime, a hydrazone or a bridged cycloalkyl group; Q' is $-\text{NO}$ or $-\text{NO}_2$; and T is independently a covalent bond, a carbonyl, an oxygen, $-\text{S}(\text{O})_o-$ or $-\text{N}(\text{R}_a)\text{R}_i-$, wherein o is an integer from 0 to 2, R_a is a lone pair of electrons, a hydrogen or an alkyl group; R_i is a hydrogen, an alkyl, an aryl, an alkylcarboxylic acid, an arylcarboxylic acid, an alkylcarboxylic ester, an arylcarboxylic ester, an alkylcarboxamido, an arylcarboxamido, an alkylsulfinyl, an alkylsulfonyl, an alkylsulfonyloxy, an arylsulfinyl, an arylsulfonyloxy, an arylsulfonyl, a sulfonamido, a carboxamido, a carboxylic ester, an aminoalkyl, an aminoaryl, $-\text{CH}_2-\text{C}(\text{T}-\text{Q}')(\text{R}_g)(\text{R}_h)$, or $-(\text{N}_2\text{O}_2-)^-\cdot\text{M}^+$, wherein M^+ is an organic or inorganic cation; with the proviso that when R_i is $-\text{CH}_2-\text{C}(\text{T}-\text{Q}')(\text{R}_g)(\text{R}_h)$ or $-(\text{N}_2\text{O}_2-)^-\cdot\text{M}^+$; then $-\text{T}-\text{Q}'$ can be a hydrogen, an alkyl group, an alkoxyalkyl group, an aminoalkyl group, a hydroxy group or an aryl group; and R_g and R_h at each occurrence are independently R_e .

91. (Previously Presented) The composition of claim 59 and at least one of L-arginine, L-homoarginine, N-hydroxy-L-arginine, nitrosated L-arginine, nitrosylated L-arginine, nitrosated N-hydroxy-L-arginine, nitrosylated N-hydroxy-L-arginine, nitrosated L-homoarginine, nitrosylated L-homoarginine), citrulline, ornithine, glutamine, lysine, an arginase inhibitor or a nitric oxide mediator.

92-111 (Cancelled)

112. (Previously Presented) A kit comprising the composition of claim 72.

113. (Previously Presented) A compound selected from the group consisting of :
1-(3-(1-(hydroxyimino)-4-(nitrooxy)butyl)-1- phenylpyrazol-5-yl)-4-(methylsulfonyl)benzene;
1-(1-cyclohexyl-3-(1-(hydroxyimino)- 4-(nitrooxy)butyl)pyrazol-5-yl)-4-(methylsulfonyl)
benzene; 1-(3-(2-aza-2-methoxy-1-(3-(nitrooxy)propyl)vinyl- 1-cyclohexylpyrazol -5-yl)-4-
(methylsulfonyl)benzene; 4-(3-(1-(hydroxyimino)-5-(nitrooxy)butyl)-4- (4-
(methylsulfonyl)phenyl)-pyrazolyl) benzenecarbonitrile; 1-(1-cyclohexyl-3-(1-(hydroximino)- 6-
(nitrooxy)hexyl)-pyrazol-5-yl)-4-(methylsulfonyl) benzene; *tert*-butyl 2-((1E)-2-{1-cyclohexyl-5-
[4-(methylsulfonyl)phenyl]pyrazol-3-yl}-5-(nitrooxy)-1-azapent-1-enyloxy)acetate; or a
pharmaceutically acceptable salt thereof.

114. (Previously Presented) A composition comprising at least one compound of claim
113 and a pharmaceutically acceptable carrier.

115. (Previously Presented) The composition of claim 114, further comprising at least
one therapeutic agent.

116. (Previously Presented) A kit comprising at least one compound of claim 113.